CLAIMS

What is claimed is:

1. A method of diagnosing a susceptibility to Type II diabetes in an individual, comprising detecting a polymorphism in a SLIT-3 nucleic acid, wherein the presence of the polymorphism in the nucleic acid is indicative of a susceptibility to Type II diabetes.

2. A method of diagnosing a susceptibility to Type II diabetes comprising detecting an alteration in the expression or composition of a polypeptide encoded by SLIT-3 nucleic acid in a test sample, in comparison with the expression or composition of a polypeptide encoded by a SLIT-3 nucleic acid in a control sample, wherein the presence of an alteration in expression or composition of the polypeptide in the test sample is indicative of a susceptibility to Type II diabetes.

3. The method of Claim, wherein the polymorphism in the SLIT-3 nucleic acid is indicated by detecting the presence of a least one of the polymorphisms indicated in FIG. 11.

4. An isolated nucleic acid molecule comprising a SLIT-3 nucleic acid, wherein the SLIT-3 nucleic acid has a nucleotide sequence selected from the group of nucleic acid sequences as shown in FIG. 10, or the complements of the group of nucleic acid sequences as shown in FIG. 10, wherein the nucleotide sequence contains a polymorphism.

5. An isolated nucleic acid molecule which hybridizes under high stringency conditions to a nucleotide sequence selected from the group of nucleic acid sequences as shown in FIG. 10, or the complements of the group of nucleic acid sequences as shown in FIG. 10, wherein the nucleotide sequence contains a polymorphism.

6. A method for assaying for the presence of a first nucleic acid molecule in a sample, comprising contacting said sample with a second nucleic acid molecule, where the second nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of: nucleic acid sequences as shown in FIG. 10 and the complement of the nucleic acid sequences as shown in FIG. 10, wherein the nucleotide sequence contains a polymorphism and hybridizes to the first nucleic acid under high stringency conditions.

7. A vector comprising an isolated nucleic acid molecule selected from the group consisting of:

a) nucleic acid sequences as shown in FIG. 10; and

b) complement of one of the nucleic acid sequences are shown in FIG. 10; and

wherein the nucleic acid molecule contains a polymorphism and is operably linked to a regulatory sequence.

8. A recombinant host cell comprising the vector of Claim 7.

9. A method for producing a polypeptide encoded by an isolated nucleic acid molecule having a polymorphism, comprising culturing the recombinant host cell of Claim 10 under conditions suitable for expression of the nucleic acid molecule.

10. A method of assaying for the presence of a polypeptide encoded by an isolated nucleic acid molecule according to Claim 4 in a sample, the method comprising contacting the sample with an antibody which specifically binds to the encoded polypeptide.

11. A method of identifying an agent that alters expression of a SLIT-3 nucleic acid, comprising:

a) contacting a solution containing a nucleic acid comprising the promoter region of the SLIT-3 nucleic acid operably linked to a reporter gene with an agent to be tested;

b) assessing the level of expression of the reporter gene; and

c) comparing the level of expression with a level of expression of the reporter gene in the absence of the agent; wherein if the level of expression of the reporter gene in the presence of the agent differs, by an amount that is statistically significant, from the level of expression in the absence of the agent, then the agent is an agent that alters expression of the SLIT-3 nucleic acid.

12. An agent that alters expression of the SLIT-3 nucleic acid, identifiable according to the method of Claim 11.

13. A method of identifying an agent that alters expression of a SLIT-3 nucleic acid, comprising:

a) contacting a solution containing a nucleic acid of Claim 1 or a derivative or fragment thereof with an agent to be tested;

b) comparing expression with expression of the nucleic acid, derivative or fragment in the absence of the agent;

wherein if expression of the nucleotide, derivative or fragment in the presence of the agent differs, by an amount that is statistically significant, from the expression in the absence of the agent, then the agent is an agent that alters expression of the SLIT-3 nucleic acid.

14. The method of Claim 13, wherein the expression of the nucleotide, derivative or fragment in the presence of the agent comprises expression of one or more splicing variant(s) that differ in kind or in quantity from the expression of one or more splicing variant(s) the absence of the agent.

15. An agent that alters expression of a SLIT-3 nucleic acid, identifiable according to the method of Claim 14.

16. An agent that alters expression of a SLIT-3 nucleic acid, selected from the group consisting of: antisense nucleic acid to a SLIT-3 nucleic acid; a SLIT-3 polypeptide; a SLIT-3 nucleic acid receptor; a SLIT-3 binding agent; a

peptidomimetic; a fusion protein; a prodrug thereof; an antibody; and a ribozyme.

17. A method of altering expression of a SLIT-3 nucleic acid, comprising contacting a cell containing a SLIT-3 nucleic acid with an agent of Claim 18.

18. A method of identifying a polypeptide which interacts with a SLIT-3 polypeptide comprising a polymorphism indicated in Table 3, comprising employing a yeast two-hybrid system using a first vector which comprises a nucleic acid encoding a DNA binding domain and a SLIT-3 polypeptide, splicing variant, or a fragment or derivative thereof, and a second vector which comprises a nucleic acid encoding a transcription activation domain and a nucleic acid encoding a test polypeptide, wherein if transcriptional activation occurs in the yeast two-hybrid system, the test polypeptide is a polypeptide which interacts with a SLIT-3 polypeptide.

19. A Type II diabetes therapeutic agent selected from the group consisting of: a SLIT-3 nucleic acid or fragment or derivative thereof; a member of the Robo family nucleic acid or fragment or derivative thereof; a polypeptide encoded by a SLIT-3 nucleic acid; a polypeptide encoded by a member of the Robo family nucleic acid; a SLIT-3 receptor; receptor for a member of the Robo family; a SLIT-3 nucleic acid binding agent; a Robo familiy member nucleic acid binding agent; a peptidomimetic; a fusion protein; a prodrug; an antibody; an agent that alters SLIT-3 nucleic acid expression; an agent that alters a Robo family member nucleic acid expression; an agent that alters activity of a polypeptide encoded by a SLIT-3 nucleic acid; ; an agent that alters activity of a polypeptide encoded nucleic acid of a Robo family member; an agent that alters posttranscriptional processing of a polypeptide encoded by a SLIT-3 nucleic acid; an agent that alters posttranscriptional processing of a polypeptide encoded by a nucleic acid of a Robo family member; an agent that alters interaction of a SLIT-3 nucleic acid with a SLIT-3 binding agent; ; an agent that alters interaction of a nucleic acid of a member of the Robo family with a Robo family binding agent; ; an agent that alters interaction of a SLIT-3 nucleic acid with a Robo family member; an agent that alters transcription of

splicing variants encoded by a SLIT-3 nucleic acid; an agent that alters transcription of splicing variants encoded by a nucleic acid of a Robo family member; and a ribozyme.

20. A pharmaceutical composition comprising a Type II diabetes therapeutic agent of Claim 19.

21. The pharmaceutical composition of Claim 20, wherein the Type II diabetes therapeutic agent is an isolated nucleic acid molecule comprising a SLIT-3 nucleic acid or fragment or derivative thereof.

22. The pharmaceutical composition of Claim 20, wherein the Type II diabetes therapeutic agent is a polypeptide encoded by the SLIT-3 nucleic acid.

23. A method of treating a disease or condition associated with SLIT-3 in an individual, comprising administering a Type II diabetes therapeutic agent to the individual, in a therapeutically effective amount.

24. The method of Claim 23, wherein the Type II diabetes therapeutic agent is a SLIT-3 nucleic acid agonist.

25. The method of Claim 23, wherein the Type II diabetes therapeutic agent is a SLIT-3 nucleic acid antagonist.

26. A transgenic animal comprising a nucleic acid selected from the group consisting of: an exogenous SLIT-3 nucleic acid and a nucleic acid encoding a SLIT-3 polypeptide.

27. A method for assaying a sample for the presence of a SLIT-3 nucleic acid, comprising:

a) contacting said sample with a nucleic acid comprising a contiguous nucleotide sequence which is at least partially complementary to a part of the sequence of said SLIT-3 gene under conditions appropriate for hybridization, and

b) assessing whether hybridization has occurred between a SLIT-3 gene nucleic acid and said nucleic acid comprising a contiguous nucleotide sequence which is at least partially complementary to a part of the sequence of said SLIT-3 nucleic acid;

wherein if hybridization has occurred, a SLIT-3 nucleic acid is present in the nucleic acid.

28. The method of Claim 27, wherein said nucleic acid comprising a contiguous nucleotide sequence is completely complementary to a part of the sequence of said SLIT-3 nucleic acid.

29. The method of Claim 27, further comprising amplification of at least part of said SLIT-3 nucleic acid.

30. The method of Claim 27, wherein said contiguous nucleotide sequence is 100 or fewer nucleotides in length and is either: a) at least 80% identical to a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in FIG. 10; b) at least 80% identical to the complement of a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in FIG. 10; or c) capable of selectively hybridizing to said SLIT-3 nucleic acid.

31. A reagent for assaying a sample for the presence of a SLIT-3 nucleic acid, said reagent comprising a nucleic acid comprising a contiguous nucleotide sequence which is at least partially complementary to a part of the nucleotide sequence of said SLIT-3 nucleic acid.

32. The reagent of Claim 31, wherein the nucleic acid comprises a contiguous nucleotide sequence, which is completely complementary to a part of the nucleotide sequence of said SLIT-3 nucleic acid.

33. A reagent kit for assaying a sample for the presence of a SLIT-3 nucleic acid, comprising in separate containers:

a) one or more labeled nucleic acids comprising a contiguous nucleotide sequence which is at least partially complementary to a part of the

nucleotide sequence of said SLIT-3 nucleic acid, and

b) reagents for detection of said label.

34. The reagent kit of Claim 33, wherein the labeled nucleic acid comprises a contiguous nucleotide sequences which is completely complementary to a part of the nucleotide sequence of said SLIT-3 nucleic acid.

35. A reagent kit for assaying a sample for the presence of a SLIT-3 nucleic acid, comprising one or more nucleic acids comprising a contiguous nucleic acid sequence which is at least partially complementary to a part of the nucleic acid sequence of said SLIT-3 nucleic acid, and which is capable of acting as a primer for said SLIT-3 nucleic acid when maintained under conditions for primer extension.

36. The use of a nucleic acid which is 100 or fewer nucleotides in length and which is either: a) at least 80% identical to a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in FIG. 10; b) at least 80% identical to the complement of a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in FIG. 10; or c) capable of selectively hybridizing to said SLIT-3 nucleic acid, for assaying a sample for the presence of a SLIT-3 nucleic acid.

37. The use of a first nucleic acid which is 100 or fewer nucleotides in length and which is either:

a) at least 80% identical to a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in FIG. 10;

b) at least 80% identical to the complement of a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in FIG. 10; or

c) capable of selectively hybridizing to said SLIT-3 nucleic acid;

for assaying a sample for the presence of a SLIT-3 nucleic acid that has at least one nucleotide difference from the first nucleic acid.

38. The use of a nucleic acid which is 100 or fewer nucleotides in length and which is either:

a) at least 80% identical to a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in FIG. 10;

b) at least 80% identical to the complement of a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in FIG. 10; or

c) capable of selectively hybridizing to said SLIT-3 nucleic acid;

for diagnosing a susceptibility to a disease or condition associated with a SLIT-3.

39. A method of diagnosing a susceptibility to Type II diabetes in an individual, comprising determining the presence or absence in the individual of a haplotype shown in Table 2 or a haplotype shown in Table 5, at the 5q35 loci, wherein the presence of the haplotype is diagnostic of susceptibility to Type II diabetes.

40. The method of Claim 39, wherein determining the presence or absence of the haplotype comprises enzymatic amplification of nucleic acid from the individual.

41. The method of claim 40, wherein determining the presence or absence of the haplotype further comprises electrophoretic analysis.

42. The method of claim 39, wherein determining the presence or absence of the haplotype further comprises restriction fragment length polymorphism analysis.

43. The method of claim 39, wherein determining the presence or absence of the haplotype further comprises sequence analysis.

44. A method of diagnosing a susceptibility to Type II diabetes in an individual, comprising:

a) obtaining a nucleic acid sample from said individual; and

b) analyzing the nucleic acid sample for the presence or absence of a haplotype shown in Table 2 or shown in Table 5, at the 5q35 loci comprising a SLIT-3 gene, wherein the presence of the haplotype is diagnostic for a susceptibility to Type II diabetes.

45. A method of diagnosing a susceptibility to Type II diabetes in an individual, comprising determining the presence or absence in the individual of a haplotype comprising one or more markers and/or single nucleotide polymorphisms as shown in FIG. 11, in the locus on chromosome 5q35, wherein the presence of the haplotype is diagnostic of a susceptibility to Type II diabetes.

46. A method for the diagnosis and identification of a susceptibility to Type II diabetes in an individual, comprising: screening for an at-risk haplotype in the SLIT-3 nucleic acid that is more frequently present in an individual susceptible to Type II diabetes compared to an individual who is not susceptible to Type II diabetes wherein the at-risk haplotype increases the risk significantly.

47. The method of Claim 46 wherein the significant increase is at least about 20%.

48. The method of Claim 46 wherein the significant increase is identified as an odds ratio of at least about 1.2.

49. Use of a Type II diabetes therapeutic agent for the manufacture of a medicament for the treatment of a disease or condition associated with SLIT-3 in an individual.

50. The use of Claim 49, wherein the Type II diabetes therapeutic agent is a SLIT-3 nucleic acid agonist.

51. The use of Claim 49, wherein the Type II diabetes therapeutic agent is a SLIT-3 nucleic acid antagonist.